REMARKS

Status of the Claims

Claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 are in the application.

Claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 were rejected.

Claims 1, 11, 12, 33, 46, 49 and 56 have been amended.

Upon entry of this amendment, claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 will be pending.

Summary of the Amendment

Claims 1, 12, 33, 46, 49 and 56 have been amended to set forth specific embodiments of the invention.

Claims 33 and 56 have also been amended to correct an obvious error with respect to a lack of antecedent basis.

Claim 11 has been rewritten to place it in allowable form.

No new matter has been added.

Claim Rejection Under 35 U.S.C. § 102

Claims 1, 6, 12, 17, 53 and 54 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent number 6,417,328 (hereinafter "Alnemri"). Applicants respectfully disagree and request that the rejection based upon 35 U.S.C. § 102(e) be withdrawn.

Alnemri does not anticipate any of claims 1, 6, 12, 17, 53 and 54.

The claims refer to "pyrogen-free compositions" that include "a nucleotide sequence that encodes an immunogen operably linked to regulatory elements" and "a nucleotide sequence that encodes an immunomodulating protein operably linked to regulatory elements". The immunomodulating protein may be the elected species DR5.

Alnemri does not expressly or inherently disclose compositions (1) that are pyrogen-free; and (2) that include a nucleic acid sequence encoding DR5; and (3) that include a nucleic acid

sequence encoding an immunogen. Nowhere in Alnemri is a composition having each of these three characteristics expressly or inherently disclosed.

Applicants respectfully urge that the passages in Alnemri relied upon by the Office to support the rejection do not disclose a composition having the three elements noted above. Rather, Alnemri includes a disclosure of a composition having the two coding sequences in one section and a disclosure of sterile compositions with one of coding sequence in another, unrelated section. The Office has improperly combined these two unrelated sections of Alnemri in order to conclude that Alnemri disclose a sterile compositions with each of the two coding sequences. Moreover, the Office has concluded that one skilled in the art would understand the description of sterile compositions to mean pyrogen-free compositions. Applicants urge that the term pyrogen-free has a particular meaning and the disclosure does not support the Office's interpretation that Alnemri discloses pyrogen free compositions.

Turning first to the improper combining the disclosure of two separate and distinct types of compositions, Applicants respectfully urge that the portion of Alnemri that discloses sterile compositions which comprise DR5 coding sequences is separate and distinct from the portion of Alnemri that discloses DR5 coding sequences in combination with immunogen coding sequences. The two sections are directed to two completely unrelated concepts and cannot be properly combined to conclude that the claimed invention is disclosed.

In the section of Alnemri that refers to sterile therapeutics, the purpose of the therapeutics is to deliver DR5 as a therapeutic protein by itself. Alnemri does not suggest including any other coding sequences. Alnemri does not provide any reason why an additional coding sequence would be included in a DR5 gene therapeutic. Alnemri discloses that DR5 coding sequences can be used to deliver DR5 polypeptide in order to diagnose, treat or reduce severity of cell mediated diseases including, but not limited to a number of listed diseases. In disclosing the use of DR5 coding sequences that would presumably include pharmaceutical compositions comprising DR5 coding sequences, Alnemri does not disclose including immunogen coding sequences. One skilled in the art would not infer from Alnemri's disclosure that the addition of immunogen coding sequences would be useful in combination with the DR5 coding sequences. In the

context of disclosing pharmaceutical compositions that include DR5 coding sequences, Alnemri is completely silent with respect to addition of immunogen coding sequences and nothing is disclosed that would suggest the desirability of making such a combination.

In the section of Alnemri which refers to DR5 coding sequences in combination with immunogen coding sequences, these gene constructs are used as laboratory reagents in apoptosis assays to study the apoptotic activity of DR5. The bacterial gene *lac* was included on a plasmid that encodes DR5. The plasmid was used to transfect cells. The percentage of blue cells (*lac* expressing cells) undergoing apoptosis with respect to the total number of blue cells was observed and reported to be in excess of 80%. Alnemri uses these data to conclude that DR5 induces apoptosis because: (1) blue cells contain both the *lac*-coding sequence and a DR5 coding sequence and (2) a large majority of blue cells are apoptotic. The *lac* gene merely serves as a reporter gene to identify which cells have been transfected with the plasmid that encodes DR5. There is no mention of this plasmid to be used in an *in vivo* assay. One of ordinary skill in the art would have no motivation to do so.

The CrmA gene encodes a viral protein with Caspase inhibitor activity. Alnemri used a CrmA coding sequence to observe the effect of Caspase inhibition on the apoptotic activity of DR5.

Alnemri reports that co-expression of CrmA and DR5 blocks apoptosis in cells that undergo apoptosis in the presence of DR5 by itself. These data allow Alnemri to conclude that caspase is involved in the DR5 apoptosis pathway. In both cases, the combination of sequences that encode DR5 and sequences that encode *lac* or CrmA were provided for use in *in vitro* experiments to study DR5-induced apoptosis.

In each case, the immunogen gene was used as a tool in an *in vitro* experiment to allow for the study of DR5 activity. Nothing in the disclosure of these experiments suggests any use of the compositions *in vivo*. As noted above, Alnemri states that DR5 coding sequences can be used to deliver DR5 to diagnose, treat or reduce severity of diseases that are mediated by increases or decreases in programmed cell death. No reason is provided or suggested which would indicate that sterile pharmaceutical compositions comprising DR5 coding sequences in

combination with immunogen coding sequences would be desirable for the uses of DR5 disclosed by Alnemri.

Applicants respectfully urge that the section describing therapeutics which include DR5 coding sequences does not include the further addition of immunogen genes disclosed in *in vivo* experiments performed to study DR5 activity. The immunogen genes were used as tools to understand the apoptotic pathway induced by DR5.

As noted in the previous response, to anticipate a claim, the prior art reference must describe the invention. That is, the art must disclose the elements "arranged as in the claim." The CAFC case cited in the previous response, *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) is particularly instructive on this point which is well settled in the law. *Net MoneyIN* cites *In re Arkley*, 455 F.2d 586, 587 (C.C.P.A. 1972) which states:

> [The] reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.

It is abundantly clear that anticipation requires the presence of every element of the claimed invention, not simply the isolated mention of different elements in different, unrelated passages.

Alnemri does not disclose the claimed invention. Alnemri does not disclose a composition: (1) that is pyrogen-free; (2) that includes a DR5 coding sequence; and (3) that includes an immungen-coding sequence as provided by the claims.

Furthermore, as previously noted, Applicants urge that Alnemri does not disclose any pyrogen-free compositions. The level of purity of a pyrogen-free composition is a much higher level of purity than the purity of a sterile composition. The compositions described in Alnemri, such as in column 23, lines 12-17, are not necessarily pyrogen-free.

In view of the foregoing, Applicants respectfully request that the rejections of claims 1, 6, 12, 17, 53 and 54 under 35 U.S.C. § 102(e) as being anticipated by Alnemri be withdrawn.

Claim Rejection Under 35 U.S.C. § 103

Claims 1, 6, 12, 17, 53 and 54 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Alnemri in view of US Pat. No. 5,693,622 (hereinafter "Wolff").

As noted above, Alnemri does not disclose any composition that is (1) pyrogen-free and comprises both (2) a DR5 coding sequence; and (3) an immunogen-coding sequence.

Wolff discloses DNA vaccines.

Nothing in Wolfe teaches or suggests the inclusion of DR5 coding sequences. Nothing in Alnemri suggests use of DR5 in vaccines. There is no teaching or suggestion of combining the two references to produce the claimed invention, either in the references themselves or anywhere else. One skilled in the art would not recognize the benefit of including DR5 coding sequences in compositions that induce immune responses against immunogens. The claimed invention is not obvious.

Applicants respectfully request that the rejection of claims 1, 6, 12, 17, 53 and 54 based upon 35 U.S.C. §103(a) be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, first paragraph

Claim 11 remains rejected under 35 U.S.C. § 112, first paragraph as allegedly failing the enablement requirement.

Claim 11 has been amended to incorporate language consistent with the claims for which the enablement rejection has been withdrawn. The amendment obviates the basis of the rejection of Claim 11.

Applicants respectfully request that the rejection of claim 11 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, second paragraph

Claims 33, 36, 52 and 55-58 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter applicants regard as the invention.

It is noted that claims 33 and 56 lack antecedent basis with respect to the recitation of "the immunomodulating protein" set forth in each of the two claims. Claims 36, 52, 55, 57 and 58 are included in the rejection as being dependent upon one of either claim 33 or 56.

Claims 33 and 56 have each been amended to correct the error in language that formed the basis of the rejection. The amendments obviate the basis of the rejection. Claims 33, 36, 52 and 55-58 are clear and definite.

Applicants respectfully request that the rejection of claims 33, 36, 52 and 55-58 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claim Objections

An objection remains to claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 for reciting non-elected subject matter.

The Office indicates that the generic claim has not been found to be allowable and accordingly, cancelation of non-elected subject matter is required. The Office further notes that is claim 7 is found allowable, an objection to claim 33 will be made as being a substantial duplicate of claim 7.

Claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 are deemed non-allowable generic claims because, upon examination of the generic claims, the following rejections have been made to the generic claims:

> Claims 1, 6, 7, 12, 17, 18, 33 and 53-57 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 96/36366 (1996; hereinafter "Dow").
>
> Claims 4, 9-11, 15, 36, 42, 43, 46, 49, 50, 52 and 58 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dow in view of US Pat. No. 6,204,250 (2001; hereinafter "Bot") and US Pat. No. 5,494,807 (1996; hereinafter "Paoletti").

Dow discloses compositions comprising sequences that encode superantigens and MCP-1, MIP-1α, MIP-1β, IL-8, and RANTES, and the uses of such compositions.

Claims 1, 12, 33, 46, 49 and 56 have been amended to delete references to MCP-1, MIP-1α, MIP-1β, IL-8, and RANTES. As amended, neither Dow nor Bot nor Paoletti teach or suggest the claimed subject matter.

Applicants respectfully request that the rejection of claims 1, 6, 7, 12, 17, 18, 33 and 53-57 under 35 U.S.C. § 102(b) as being anticipated by Dow and the rejection of claims 4, 9-11, 15, 36, 42, 43, 46, 49, 50, 52 and 58 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dow in view of Bot and Paoletti, be withdrawn.

As amended, the generic claims are allowable.

Applicants respectfully request that the objection to claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 for reciting non-elected subject matter be withdrawn.

With respect to the prospective objection to claim 33 in view of allowable claims 7, Applicants respectfully note that the claims are not substantial duplicates of each other. Claim 7 refers to immunogens while claim 33 limits the immunogen to pathogen antigens. One skilled in the art would immediately recognize the difference in scope of the claims and conclude that the two claims are not duplicative.

Conclusion

Claims 1, 4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 46, 49, 50 and 52-58 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7855 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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